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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/963,299	09/26/2001	Alejandro Abuin	LEX-0246-USA	3043

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EXAMINER	
PARAS JR, PETER	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 02/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/963,299	ABUIN ET AL.	
	Examiner	Art Unit	
	Peter Paras, Jr.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 8 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 8 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 September 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *0402*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment received on 12/8/03 has been entered. Claim 8 has been amended. Claims 1-7 and 9 have been cancelled. Claim 8 is pending and is under current consideration.

Drawings

The drawing filed on 9/26/01 is approved.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-7 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

The claims are further directed to a murine embryonic stem cell line comprising an engineered mutation in a gene comprising the nucleotide sequence set forth in SEQ ID NO: 36.

The instant specification has disclosed novel cDNA sequences produced using gene trap technology. See the specification at page 7. The claims embrace a murine embryonic stem cell line having a mutation in a gene comprising the nucleotide sequence disclosed in SEQ ID NO: 36. The instant specification has discussed that such embryonic stem cells can be used for creating transgenic animals, screening

assay to identify compounds that may act to ameliorate developmental or cell differentiation disorder systems, gene discovery, and production of mutated proteins. See pages 12-15 of the specification. However, the evidence of record does not provide a correlation between the nucleotide sequence set forth in SEQ ID NO: 36 and any gene which comprises the nucleotide sequence set forth in SEQ ID NO: 36 or protein product that it encodes. Moreover, while the specification has purported that the nucleotide sequence set forth in SEQ ID NO: 36 is contained within a gene, the specification has not disclosed which gene may contain said nucleotide sequence or which protein (and its function) is encoded by such a gene. In addition, the specification has failed to establish a relationship between the polynucleotide of SEQ ID NO: 36 and any specific disease or establish any involvement of the polynucleotide of SEQ ID NO: 36 in the etiology of any specific disease. Since SEQ ID NO: 36 lacks a correlation to any known gene or disease it would not be possible to predict a phenotype related to a transgenic mouse comprising a disruption in a gene comprising SEQ ID NO: 36.

A substantial utility is a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities under §101. Applicant's specification fails to provide a "real world" use of a gene that comprises the nucleotide sequence set forth in SEQ ID NO: 36 such that the a murine embryonic stem cell comprising a disruption in such a gene additionally has no "real world" use. Neither the specification as filed, nor any art of record disclose or suggest any biological or biochemical activity for the protein

encoded by such a gene such that any utility would be well established for the protein. The asserted utilities for SEQ ID NO: 36 such as a probe for diagnosing a disease, primers for PCR, treatment of disease, identification of coding sequences, creation of transgenic animals, production of proteins are merely "potential" uses that apply to any uncharacterized, unrelated polynucleotide sequences. Therefore the asserted utilities are not considered "specific" utilities, i.e. they are not specific to SEQ ID NO: 36. As such an unidentified gene comprising the nucleotide sequence of SEQ ID NO: 36 or a murine ES cell comprising a disruption in such an identified gene also lack specific utilities.

The asserted utility of a murine ES cell comprising a disruption in a gene containing SEQ ID NO: 36 is based on the assertion that SEQ ID NO: 36 is a part of a gene. The specification has not provided any information regarding which gene may contain SEQ ID NO: 36, which protein (and its function) is encoded by the gene or which disease is related to SEQ ID NO: 36. As such a specific and substantial utility for SEQ ID NO: 36 has not been provided by the evidence of record. Accordingly, an ES cell comprising a disruption in a gene containing SEQ ID NO: 36 also lacks a specific and substantial utility. Finally, a transgenic mouse comprising an ES cell that comprises a disruption in a gene containing SEQ ID NO: 36 would have not any apparent or predictable phenotype since the function of the protein encoded by such a gene is unknown. In the absence of any apparent phenotype, a transgenic mouse would have no obvious utility that is substantial and specific.

In view of the above it appears that the he specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the nucleotide sequence set forth in SEQ ID NO: 36 and murine ES cells comprising a disruption in SEQ ID NO: 36. In view of the lack of guidance with respect to the gene containing SEQ ID NO: 36, the claimed invention encompasses, the skilled artisan would not know how to use such a gene, its expression product, a murine ES cell comprising a disruption in such a gene, or a transgenic mouse comprising such an ES cell. Because the claimed invention as a whole is not supported by a specific and substantial asserted utility for the reasons set forth, credibility of any utility cannot be assessed.

Claims 1-7 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

In addition to the above issues, the claims as written are subject to an additional enablement rejection as set forth below.

The claims embrace murine ES cells comprising a mutation is a gene comprising the nucleotide sequence set forth in SEQ ID NO: 36. The term murine encompasses animals other than mice, such as rats. The specification has contemplated that such ES cells may be used to create transgenic animals. See pages 12-15. Currently, the state of the transgenic art regarding ES cell technology for the production of transgenic animals other than mice is undeveloped. This is because ES cell technology is

generally limited to the mouse system and that only "putative" ES cells exist for other species. See Moreadith et al. at page 214, Summary. Seamark (Reproductive Fertility and Development, 1994) supports this observation by reporting that totipotency for ES cell technology in many livestock species has not been demonstrated (page 6, Abstract). Likewise, Mullins et al. (Journal of Clinical Investigation, 1996) state that "although to date chimeric animals have been generated from several species including the pig, in no species other than the mouse has germline transmission of an ES cell been successfully demonstrated." (page S38, column 1, first paragraph). The state of the art does not support the use of rat embryonic stem cells for creating knockout rats. Furthermore, the instant specification has failed to provide guidance correlating to the use of non-mouse ES cells.

Given the unpredictable and undeveloped state of the ES cells art it would have required undue experimentation for the skilled artisan to create transgenic knockout of murine species other than mouse.

Claim 1-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are further directed to a murine embryonic stem cell line comprising an engineered mutation in a gene comprising the nucleotide sequence set forth in SEQ ID NO: 36.

The genes comprising the nucleotide sequence set forth in SEQ ID NO: 36 encompassed within the genus have not been disclosed. Based upon the prior art there is expected to be variation among the species of genes within the genus, because the gene species would be expected to vary among individuals. The specification discloses isolation of a nucleotide sequence (SEQ ID NO: 36) from mouse ES cells and purports that SEQ ID NO: 36 is part of the coding sequence from a gene. There is no evidence on the record of a relationship between the structure of any gene and the sequence set forth in SEQ ID NO: 36 that would provide any reliable information about the structure of any gene within the genus. There is no evidence on the record that the nucleotide sequence set forth in SEQ ID NO: 36 had a known structural relationship to any gene sequence. Moreover, the structural elements of a gene comprising SEQ ID NO: 36 such as regulatory regions, intron-exon boundaries, and 3' regions have not been disclosed. In view of the above considerations one of skill in the art would not recognize that applicant was in possession of the necessary common features or attributes possessed by member of the genus, because partial coding sequence as set forth in SEQ ID NO: 36 is not representative of any gene within the claimed genus. Consequently, since Applicant was in possession of only a partial coding sequence of a gene, the nucleotide sequence set forth in SEQ ID NO: 36 was not representative of the claimed genus. Therefore, Applicant was not in possession of the genus of gene

comprising the nucleotide sequence set forth in SEQ ID NO: 36 as encompassed by the claims. University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that to fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention."

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 is indefinite as written. The claim embraces a gene identifiable as encoding the polynucleotide sequence of SEQ ID NO: 36. The claim is indefinite because a gene doesn't encode a polynucleotide sequence. Genes are normally known to encode proteins. Appropriate correction is required. The following claim language is suggested to overcome the instant rejection: "a gene identifiable as [having] or [comprising] the polynucleotide sequence set forth in SEQ ID NO: 22".

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Peter Paras, Jr., whose telephone number is (571) 272-0732. The examiner can normally be reached Monday-Friday from 8:30 to 4:30 (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at 571-272-0804. Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Official Fax Center number is (703) 872-9306.

Inquiries of a general nature or relating to the status of the application should be directed to Dianiece Jacobs whose telephone number is (571) 272-0532.

Peter Paras, Jr.

Art Unit 1632

PETER PARAS
PATENT EXAMINER